

Remarks

I. Status of the Application and Claims

A originally filed, the present application had 11 claims. These were cancelled in a Preliminary Amendment and new claims 12-31 were added. In response to a restriction requirement, claims 22-31 were cancelled and new claims 32-41 were added. The remaining claims, 12-21 and 32-41 were cancelled herein and new claims 42-62 have been added.

II. The Amendments

Claims were amended in to increase clarity. References to an "enantiomer-enriched α -hydroxycarboxylic acid" and an "enantiomer-enriched α -hydroxycarboxylic amide" were eliminated and, instead, claims now simply refer to methods of producing α -hydroxycarboxylic acids or amides. The reason for this change is that Applicants believe that the original wording may have been somewhat confusing because it is actually the compositions containing the compounds, not the compounds themselves, that are enantiomerically enriched.

Reactions for the production of acids and reactions for the production of amides have been put into separate claims and text has been added to indicate that the enzymes used in reactions act in an enantioselective manner. Support for the latter amendment may be found on page 6 of the specification, line 32 - page 7, line 3, and on page 7, lines 22-29. Applicants have also added an isolation step to claims and specify that reactions occur in a single reaction mixture. Support for these amendments may be found on page 5, lines 14-23 and page 14, lines 4-24.

Applicants believe that all of the other elements in the amended claims are supported by claims that have now been cancelled.

None of the amendments add new matter to the application and their entry is therefore respectfully requested.

The Rejections

I. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

On pages 2-3 of the Office Action, all pending claims are rejected as failing to meet the requirements of 35 USC §112, second paragraph. The Examiner alleges that the claims are vague and indefinite because process steps are omitted and because the phrase "reacting a cyanide donor with an aldehyde or ketone" is indefinite. In addition, claim 17 is alleged to be indefinite because it does not make it clear that Applicants intended to require that enzymes be derived from the biological sources recited in the claim.

In response, Applicants have amended claims in a way that they believe should be sufficient to meet the requirements of 35 USC §112. Claims now specify that the reaction between aldehydes or ketones and a cyanide donor is an enzymatic reaction catalyzed by an oxynitrilase and that a cyanohydrin is made. An isolation step has been added to complete the process and, in dependent claims, text has been changed to clarify that oxynitrilases are isolated from almond kernels or from a species selected from *Sorghum bicolor*, *Hevea brasiliensis*, or *Mannihot esculenta*. In light of these changes Applicants respectfully request that the Examiner reconsider and withdraw the present rejection.

II. Rejection of Claims Under 35 USC §103

On pages 3-5 of the Office Action, all pending claims are rejected under 35 USC §103 based upon Griengl, *et al.* (*Trends Biotech.* 18:252-256 (2000)) Nagasawa, *et al.*, (*Eur. J. Biochem.* 267:138-144 (2000)) and Osprian, *et al.* (*J. Mol. Catal. B Enz.* 24-25:89-98 (2003)). The Examiner alleges that Griengl teaches the production of enzymatically enriched cyanohydrins by reacting aldehydes or ketones with cyanide in the presence of oxynitrilases. Nagasawa is cited as teaching that nitrilases can be used to convert nitriles to carboxylic acids and Osprian as suggesting the nitrile hydratase/amidase reaction combination. The Examiner alleges that one of skill in the art would have been motivated to combine these references in order to arrive at an efficient catalytic process and that all of the other elements of Applicants' claims would have become apparent in the course of optimizing the process.

Applicants respectfully traverse this rejection.

Applicants do not dispute the Examiner's assertions concerning the reactions that are taught by the individual references. However, the references do not teach that the various reactions disclosed could be combined and carried out concurrently a single reaction mixture. The fact that prior art teachings can be combined or modified to arrive at an invention does not make the invention obvious unless the results produced would have been predictable to one of ordinary skill in the art (MPEP §2143). The success of combining enzymatic reactions into a single reaction mixture can rarely be reasonably expected and this is especially true in cases where one reaction utilizes compounds (cyanides) that act as inhibitors for a wide range of enzymes. In this regard, Applicants have enclosed herewith two references that were available prior to Applicants' filing date that suggest that cyanides inhibit nitrile hydratases.

In discussing the enzymatic activity of nitrile hydratases from two microorganisms, the first of these, US 5,866,379, states in col. 7, lines 33-46:

The observed substrate inhibition appears to be at least partially caused by the presence of free hydrogen cyanide in the nitrile feed liquid (typically ranging from about 0.25% to 1% by weight--about 1% to about 5% by mole--relative to nitrile). While some lesser amount of the corresponding aldehyde is also typically present in the nitrile feed, the hydrogen cyanide is the more significant inhibiting contributor; the aldehyde has little, if any, inhibiting effect. (Example 7).

As such, the α -hydroxynitrile substrate and/or a solution comprising the substrate is preferably treated to reduce the amount of hydrogen cyanide present during the reaction, thereby minimizing the degree of cyanide inhibition of the nitrile hydratase activity.

The second reference (US 6,043,061) states in the first paragraph under the Summary of the Invention section:

The present inventors have conducted extensive study and research efforts in order to solve the above-described problem. As the result, it could be found that a trace amount of hydrocyanic acid included in a composition containing a nitrile compound accelerated the deactivation of the enzyme nitrile hydratase. Further, it could be also found that by utilizing such composition comprising a reduced amount of hydrocyanic acid, the deactivation of the enzyme was lowered so that an amide compound could be efficiently produced from the nitrile compound, that is, by utilizing a smaller amount of the enzyme, a larger amount of an amide compound could be produced. Thus, the present invention was achieved.

The '379 and '061 patents provide direct evidence that combining a reaction in which cyanide compounds are present with a reaction in which cyanide compounds are not present and carrying them out concurrently in a single reaction mixture could not have been reasonably be predicted to result in a more efficient process. In the case of reactions involving nitrile hydratases, the patents provide evidence that there were teachings in the art that combining the oxynitrilase reaction with the nitrile hydratase reaction would *not* be expected to produce a more efficient overall process because of enzymatic inhibition caused by cyanide. Applicants' findings contradict these teachings and should, at a minimum, be nonobvious.

Conclusion

In light of the considerations above, Applicants believe that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims now pending be allowed. Early notice to this effect is earnestly solicited.

If, in the opinion of the Examiner, a phone call would help to expedite the prosecution of this application, the Examiner is invited to call Applicants' undersigned attorney at (240) 683-6165.

Respectfully submitted,
LAW OFFICE OF MICHAEL A. SANZO, LLC

By Michael A. Sanzo
Michael A. Sanzo
Reg. No. 36,912
Attorney for Applicants

Date: August 8, 2008
15400 Calhoun Drive, Suite 125
Rockville, Md. 20855
(240) 683-6165